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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/405,940	09/27/1999	JENNIFER L. HILLMAN	PF-0346-1-DI	1067

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EXAMINER	
EWOLDT, GERALD R	
ART UNIT	PAPER NUMBER
1644	23

DATE MAILED: 07/01/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/405,940	Applicant(s) Hillman et al.
	Examiner G.R. Ewoldt, Ph.D.	Art Unit 1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Dec 16, 2002*

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1, 2, 13, and 24-26* is/are pending in the application.

4a) Of the above, claim(s) *24-26* is/are withdrawn from consideratio

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1, 2, and 13* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examine

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Claims 1, 2, and 13 are being acted upon.

2. Applicant's amendment and response, filed 12/16/02, is acknowledged.

3. The specification is objected to for the introduction of new matter into the specification. In the amendment filed 12/16/02, Applicant removed from the specification the source of the TONGTUT01 cDNA library. Absent an acceptable explanation, said removal is improper and considered to be the introduction of new matter.

Correction is required in response to this action.

4. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

5. Claims 1, 2, and 13 stand rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility, for the reasons set forth in Papers No. 7, 10, and 20, mailed 10/24/00, 4/04/01, and 9/09/02, respectively.

Applicant's arguments, filed 12/16/02, have been fully considered but they are not persuasive. Applicant has provided almost thirty pages of arguments citing at least a dozen different court decisions in support of the assertion that the protein encoded by the EST of the instant claims has a patentable utility. It seems that there exist two points which must be addressed. First, do the combined EST fragments of the specification actually encode a human T cell receptor β subunit (TCRLP), and second, if so, does the instant specification establish either a specific and substantial asserted utility or a well-established utility for said T cell receptor β subunit?

In view of similarity of the claimed polypeptide that could be assembled from the translation of the combined EST fragments of the specification to known T cell receptor β subunits, the rejection as it is based on the first point, i.e., that the protein encoded by Applicant's combined ESTs is not likely a T cell receptor β subunit, has been withdrawn. Accordingly, only the arguments as they relate to the utility of said polypeptide will be addressed.

Applicant begins with a section entitled "The Applicable Legal Standard". It appears that this section is intended to address the second pertinent question, i.e., assuming *arguendo* that the combined EST fragments of the specification actually encode a human T cell receptor β subunit (TCRLP), does the instant specification establish either a specific and substantial asserted utility or a well-established utility for said protein? Applicant begins by citing numerous legal decisions.

It is unclear just how the bulk of the cited decisions could be seen to support the invention of the instant claims. For example, *Juicy Whip Inc. v. Orange Bang Inc.* involves a decision on the utility of a deceptive beverage dispenser. *Standard Oil Co. v. Montedison* involves the utility standards as they apply to the breadth of terms reciting "consisting essentially of" and "having". Other cases, such as *Nelson v. Bowler* and *In re Langer*, involve the utility of inventions for which *in vivo* data has been presented in support (these situation are certainly not analogous to the instant situation in which even *in vitro* data is lacking). And in regard to *Cross v. Iizuka*, the decision is misrepresented in such a way as to make it appear to support the instant arguments when in fact it does not (the decision does not say that the specificity requirement is met unless the asserted utility amounts to a "nebulous expression" such as "biological activity" or "biological properties", the decision merely indicates that such disclosed uses do not impart utility).

One case, however, (cited repeatedly by Applicant) seems to be particularly appropriate in defining just what is "useful", i.e., what has utility, in a relevant context. In the instant case Applicant argues that the value of the instant protein would be due to it's similarity to a known protein. Yet in *Brenner v. Manson*, 383 U.S. 519,532 (1966) the court concurred with the position of the Board of Appeals that "It is our view that the statutory requirement of usefulness of a product cannot be presumed merely because it happens to be closely related to another compound which is shown to be useful." While the claims in question recited a process, the court found that neither a product nor a process of making said product, were considered useful simply because "the compound yielded belongs to a class of compounds now under serious scientific investigation." And in the now famous and often quoted conclusion, it was set forth that "But a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion." It would seem then that even if the T cell receptor β subunit exists

and is related to another T cell receptor β subunit, the relationship would not necessarily render the instant protein patentably distinct.

Applicant asserts, "The Patent Examiner's primary rejection of the claimed invention is based on the ground that, without information as to the precise "biological role" of the claimed invention, the claimed invention's utility is not sufficiently specific. According to the Examiner, it is not enough that a person of ordinary skill in the art could use and, in fact, would want to use the claimed invention either by itself or in a 2-D gel or western blot to monitor the expression of genes for such applications as the evaluation of a drug's efficacy and toxicity. The Examiner would require, in addition, that the applicant provide a specific and substantial interpretation of the results generated in any given expression analysis."

It is unclear to the Examiner how Applicant has come to the aforestated conclusion. The Examiner has not required any interpretation of any results of any expression analysis studies. It is merely the Examiner's position that the specification fails to set forth either a specific and substantial asserted utility or a well-established utility as is required by statute.

Applicant argues, "The use of proteins expressed by humans as tools for toxicology testing, drug discovery, and the diagnosis of disease are "well-established" utilities for the claimed invention.

It is the Examiner's position that specification fails to establish that the claimed polypeptide has a well established utility as set forth by the specification. In this regard, the *total* disclosure of the specification is as follows:

"In another embodiment of the invention, TCRLP, its catalytic or immunogenic fragments or oligopeptides thereof, can be used for screening libraries of compounds in any of a variety of drug screening techniques. The fragment employed in such screening may be free in solution, affixed to a solid support, borne on a cell surface, or located intracellularly. The formation of binding complexes, between TCRLP and the agent being tested, may be measured."
"Another technique for drug screening which may be used provides for high throughput screening of compounds having suitable binding affinity to the protein of interest as described in published PCT application W084/03564. In this method, as applied

to TCRLP large numbers of different small test compounds are synthesized on a solid substrate, such as plastic pins or some other surface. The test compounds are reacted with TCRLP, or fragments thereof, and washed. Bound TCRLP is then detected by methods well known in the art. Purified TCRLP can also be coated directly onto plates for use in the aforementioned drug screening techniques. Alteratively, non-neutralizing antibodies can be used to capture the peptide and immobilize it on a solid support." "In another embodiment, one may use competitive drug screening assays in which neutralizing antibodies capable of binding TCRLP specifically compete with a test compound for binding TCRLP. In this manner, the antibodies can be used to detect the presence of any peptide which shares one or more antigenic determinants with TCRLP."

Other than as a pharmaceutical for the treatment or prevention of essentially all known cancers, this is the *entire* disclosure of the specification as regards the uses of the claimed polypeptide. Applicant's attempt to establish a utility for the polypeptide of the claims by citing numerous post-filing references , i.e., Rockett et al., Nuwaysir et al., Steiner et al., Borrebaeck et al., and Page et al., cannot overcome the facts that the *specification* does not support the now asserted utility.

Also note that even today "drug discovery" by "expression profiling", is not a routine task (as would be suggested by Applicant's arguments):

"For discovery of therapeutics to control disease, a need to go beyond identification of disease-causing genes and proteins has begun to be recognized (30). The biological incentive and desired outcome of drug intervention is just that, the intervention in the disease process or pathology. Thus, improvement of data sets to include information on causation of disease, unfortunately, still does not address the key to identify and select drug targets, namely biologic control functions. The evidence is growing that the identification of disease-causing genes has not proven to facilitate identification of viable small molecule drug targets. One clear example, reviewed recently (30), can be found in the hereditary breast cancer genes Brca1 and Brca2, which may be excellent for diagnostics, but so far have failed for therapeutics. Unfortunately, the problem is exacerbated by low predictability of *in vitro* cell models and model organisms for gene and protein roles even in animal disease models and even lower predictability for human disease." Lu, P.Y., et al., Preclinica March/April

2003, pages 35-36.

Applicant asserts "Although, the Office has acted to "enter" the Furness Declaration (Office Action of September 9,2002, p. 2, ¶I.), the Office has refused consideration of the Furness Declaration"

This assertion is factually incorrect. Neither was the declaration "discounted" nor "disregarded" as asserted by Applicant. The declaration was considered, however, it was not found sufficient to require the withdrawal of the rejections, as set forth in the previous action.

Applicant asserts, "The Declaration of Lars Michael Furness provides direct proof of the utility of the claimed invention."

Regarding Mr. Furness's declaration, Mr. Furness merely speculates that "a person skilled in the art who read the Hillman '097 application on July 18,1997 would have understood that application to disclose the SEQ ID NO:1 polypeptide to be highly useful in analysis of differential expression of proteins. For example, the specification of the Hillman '097 application would have led a person skilled in the art in July 1997 who was using protein expression monitoring in connection with working on developing new drugs for the treatment of cancer and autoimmune disorders, to conclude that a 2-D PAGE map that used the substantially purified SEQ ID NO:1 polypeptide would be a highly useful tool and to request specifically that any 2-D PAGE map that was being used for such purposes utilize the SEQ ID NO:1 polypeptide sequence. Expressed proteins are useful for 2-D PAGE analysis in toxicology expression studies for a variety of reasons, particularly for purposes relating to providing control for the 2-D PAGE analysis, and for identifying sequence or post-transnational variants of the expressed sequences in response to exogenous compounds."

Note the lack of any *specific* uses for the polypeptide of the instant specification. Mr. Furness merely expands page after page on the value of 2-D gel electrophoretic mapping technology, however, there are no specifics on how the protein encoded by the combined ESTs of the specification would be used in said technology and regardless, said technology was not disclosed in the specification.

In total, the assertions set forth by Mr. Furness add little to the patentability of the instant invention in that they comprise little more than expanded reiterations of the vague assertions of the specification, i.e., the declaration provides no specifics: no specific assays for any specific purposes, nor any specific diseases or conditions for which the polypeptide of the claims might be used in diagnosis or treatment. Regarding 2D electrophoretic mapping technology, said utility is again not specific and regardless, said utility is not disclosed in the specification.

It must also be noted that Mr. Furness's declaration can be viewed as his legal opinion of the utility standards applied in the instant rejection. The MPEP, however, specifically sets forth that a declarant's "opinion as to a legal conclusion is not entitled to any weight", see MPEP 716.01(d) OPINION EVIDENCE. Accordingly, for that reason alone, the declaration could be found not to be convincing in establishing either a specific and substantial asserted utility or a well-established utility for the invention of the instant claims.

It appears that Applicant is attempting to establish a utility for the claimed invention some 6+ years post-filing. While Applicant might argue that the now disclosed uses would have been well known at the time of filing, such an argument would not be considered credible for the following reason. Applicant saw the necessity of disclosing in the jumbo specification minute details of routine and mundane tasks such as DNA sequencing, i.e., specific enzymes to be used, or the specific promoters to be used in protein expression. It would seem inconsistent to then argue that the details of state-of-the-art technologies such as 2-D gel electrophoresis for drug discovery would have been well known or routine and therefore not requiring of inclusion in the specification. Note that in *Kawai v. Metlesics*, 480 F.2d 880, 178 USPQ 158 (CCPA 1973)it was decided that the invention is that which is disclosed in the specification at the time of filing, i.e., the specification must provide the invention's utility. As set forth above, the specification provides essentially no specifics regarding the utility of the claimed polypeptide. Applicant's post-filing arguments cannot now provide what the specification lacks.

Applicant argues "Because there is a substantial likelihood that the claimed TCRLP is functionally related to T-cell receptor beta polypeptide, a polypeptide of undisputed utility, there is by implication a substantial likelihood that the claimed

polypeptide is similarly useful. Applicants need not show any more to demonstrate utility. *In re Brana*, 51 F.3d at 1567.

A review of *In re Brana* makes it clear that the facts of that case bare little similarity to the facts in the instant case. The question in *Brana* was whether or not positive *in vitro* test results using a lymphocytic leukemia model were sufficient to support a utility as an anti-lymphocytic leukemia agent. In the instant case there are *no* test results and indeed, the specification provides only a laundry list of cancers which administration of the polypeptide of the specification might treat or prevent, i.e., cancers, including but not limited to "adenocarcinoma, leukemia, lymphoma, melanoma, myeloma, sarcoma, and teratocarcinoma and particularly cancers of the adrenal gland, bladder, bone, brain, breast, cervix, gall bladder, gastrointestinal tract, heart, kidney, liver, lung, ovaries, pancreas, paragangliomas, parathyroid, pituitary gland, prostate, salivary gland, spleen, stomach, thymus, thyroid, testes, and uterus." One of skill in the art would likely find these assertions to fly in the face of biomedical reality.

Applicant provides several pages of arguments which can be summarized as indicating that Applicant has taken the position that the Office's policy and Training Materials are inconsistent with the law.

Applicant is advised that the instant rejection is based on the Examiner's position that the brief sections of the specification devoted to uses of the claimed polypeptide (set forth in their entirety above) do not disclose either a specific and substantial asserted utility or a well-established utility as is required by the statute.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1, 2, and 13 stand also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by a credible utility, for the reasons set forth above, one skilled in the art would not know how to use the claimed invention so that it would operate as intended without

undue experimentation, for the reasons set forth in Papers No. 7, 10, and 20, mailed 10/24/00, 4/04/01, and 9/09/02, respectively.

Applicant's arguments, filed 2/16/02, have been fully considered but they are not persuasive. Applicant argues that "To the extent that the rejection under § 112, first paragraph, is based on the improper allegation of lack of patentable utility under § 101, it fails for the same reasons."

See the Examiner's response in the previous section.

8. Claim 2 stands rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention, for the reasons set forth in Papers No. 7, 10, and 20, mailed 10/24/00, 4/04/01, and 9/09/02, respectively.

Applicant's arguments, filed 12/16/02, have been fully considered but have not been found convincing. Applicant reiterates the disclosure and asserts, "Therefore, the specification provides an adequate written description of the claimed variants of SEQ ID NO:1 to convey with reasonable clarity to those skilled in the art that applicants were in possession of the invention as claimed at the time of the filing of this application."

As there does not appear to be any argument but just a reiteration of the specification, it remains the Examiner's position that the specification still fails to provide sufficient written description of the claimed polypeptides. Note that the addition of functional language does not necessarily provide an adequate written description when the specification fails to provide any guidance as to which residues of a protein might be varied and which residues must remain constant. The genus still encompasses a virtually unlimited number of proteins and it is additionally noted that the specification still fails to demonstrate that even the unvaried polypeptide of SEQ ID NO:1 has the required IL-2 inducing activity. Thus, the specification fails to disclose even a single species of the claimed genus.

9. Applicant takes issue with the invention of the claims being referred to as an EST. The invention of the instant claims is actually a polypeptide that might be encoded by an undisclosed combination of multiple EST fragments disclosed in the

specification.

10. No claim is allowed.

11. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (703) 308-9805 The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 at 703-872-9306 (before final) and 703-872-9307 (after final).

G.R. Ewoldt, Ph.D.
Primary Examiner
Technology Center 1600
June 26, 2003